IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: James G. Wetmur et al.	
Serial No. Not Yet Assigned	Group Art Unit: Not Yet Known
Filed: Herewith	Examiner: Not Yet Known
Title: **BRANCH MIGRATION OF NUCLEOTIDES**	**Prev. Art Unit: 1656** **Prev. Ex'r: Eggerton A.Campbell, Ph.D.**

FILED BY EXPRESS MAIL

Honorable Commissioner
of Patents and Trademarks
Washington, D.C. 20231

PRELIMINARY AMENDMENT ACCOMPANYING REQUEST FOR CONTINUATION APPLICATION UNDER 37 C.F.R. §1.53(b)

Dear Sirs:

Prior to examination on the merits, please enter the following amendments in the above-identified application, which is a continuation of U.S. Patent Application Serial No. 09/387,300, filed on August 31, 1999, now allowed.

EXPRESS MAIL CERTIFICATE

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Ronald C. Fedus
Reg. No. 32,567

JULY 3 2001
Date

Enz-49(P2)(C)

AMEND THIS APPLICATION AS FOLLOWS

In The Title:

Change the title of the invention to:

-- NUCLEIC ACID DISPLACER COMPOSITIONS
AND CELLS COMPRISING SAME --

In The Specification:

Page 1, line 1, before "BACKGROUND OF THE INVENTION" insert the following:

-- CROSS-REFERENCE TO OTHER RELATED APPLICATIONS

This application is a continuation of U.S. Patent Application Serial No. 09/387,300, filed on August 31, 1999, now allowed but not yet issued, which application is a continuation of U.S. Patent Application Serial No. 08/480,00, filed on June 7, 1995, which issued as U.S. Patent No. 5,958,681 on September 28, 1999, said Serial No. 08/480,000 being a continuation of U.S. Patent Application Serial No. 07/499,938, filed on March 26, 1990, abandoned. --

In The Claims

Cancel claim 1.

Add new claims 117- 178 as follows:

-- 117. (NEW) A nucleic acid displacer composition which comprises an oligo- or polynucleotide displacer which binds to or complexes with a recipient polynucleotide, said oligo- or polynucleotide displacer comprising two or more sequences:

a) at least one first sequence which binds or complexes with said recipient polynucleotide;

b) at least one second sequence, said second sequence:

(i) being complementary or identical to at least a portion of said recipient polynucleotide; and

(ii) comprising one or more nucleotides which are different

wherein said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide. --

-- 118. (NEW) The composition of claim 117, wherein said second sequence is adjacent to said first sequence. --

-- 119. (NEW) The composition of claim 117, wherein said second sequence is separated from said first sequence by from 1 to 5 intervening moieties. --

-- 120. (NEW) The composition of claim 119, wherein one of said intervening moieties has an intercalating agent covalently attached thereto. --

-- 121. (NEW) The composition of claim 119, wherein said intervening moieties are nucleotides. --

-- 122. (NEW) The composition of claim 120, wherein at least one of said moieties is a modified nucleotide. --

-- 123. (NEW) The composition of claim 122, wherein said modified nucleotide has an intercalating agent covalently attached. --

-- 124. (NEW) The composition of claim 122, wherein said modified nucleotide is incapable of base pairing. --

-- 125. (NEW) The composition of claim 117, wherein at least one of said nucleotides complementary to one strand of the recipient polynucleotide is modified to increase the stability of the displacer-recipient complex, wherein the modification is in the second sequence. --

-- 126. (NEW) The composition of claim 117, wherein at least one of said nucleotides complementary to one strand of a recipient polynucleotide duplex is modified to increase the melting temperature of the displacer-recipient complex. --

-- 127. (NEW) The composition of claim 125, wherein said modified nucleotides comprise modified nucleotides which increase the association constant with the complementary nucleotide by at least about 20 percent. --

-- 128. (NEW) The composition of claim 125, wherein said modified nucleotides comprise modified nucleotides which increase the association constant with the complementary nucleotide by at least about 70 percent. --

--129. (NEW) The composition of claim 125, wherein at least about 10% of the nucleotides in said second sequence is modified. --

-- 130. (NEW) The composition of claim 129, wherein said modification has been carried out on a modified nucleotide is selected from the group consisting of 5-halogenated pyrimidine nucleotides, 5-methyldeoxycytidine, diaminopurine deoxynucleotide, ribonucleotides and 2'-alkylated ribonucleotides. --

-- 131. (NEW) The composition of claim 129, wherein said modified nucleotide comprises a 5-halogenated pyrimidine nucleotide. --

-- 132. (NEW) The composition of claim 129, wherein said modified nucleotide comprises 5-bromodeoxyuridine. --

-- 133. (NEW) The composition of claim 129, wherein said modified nucleotide comprises 5-methyldeoxycytidine. --

-- 134. (NEW) The composition of claim 117, which further comprises at least one moiety attached to a terminus of the oligo or polynucleotide, said moiety conferring endonuclease resistance to the terminus to which it is attached. --

-- 135. (NEW) The composition of claim 134, wherein said moiety is attached to a terminal nucleotide. --

-- 136. (NEW) The composition of claim 135, wherein said moiety is indirectly attached to a terminal nucleotide. --

-- 137. (NEW) The composition of claim 134, wherein said moiety is attached to the deoxyribose moiety at the hydroxyl group of a terminal nucleotide. --

-- 138. (NEW) The composition of claim 134, wherein said moiety is attached to the phosphate moiety of a terminal nucleotide. --

-- 139. (NEW) The composition of claim 134, where said moiety is selected from the group consisting of intercalating agents, isoureas, carbodiimides and N-hydroxybenzotriazoles. --

-- 140. (NEW) The composition of claim 137, wherein said moiety comprises a methylthiophosphonate. --

-- 141. (NEW) The composition of claim 134, wherein said moiety is selected from the group consisting of polypeptides and proteins. --

-- 142. (NEW) The composition of claim 134, wherein said moiety is a 2',3'-dideoxyribose nucleotide attached to the 3'-terminal nucleotide through a phosphodiester linkage. --

-- 143. (NEW) The composition of claim 142, wherein said 2',3'-dideoxyribose nucleotide comprises a modified 2',3'-dideoxyribose nucleotide. --

-- 144. (NEW) The composition of claim 117, further comprising a modification which permits detection of the displacer-recipient complex. --

-- 145. (NEW) The composition of claim 144, wherein said modification comprises a member selected from the group consisting of non-radioactive labels, radioactive labels, fluorescent labels , chemiluminescent labels, enzymes and targets for detection. --

-- 146. (NEW) The composition of claim 144, wherein said modification is selected from the group consisting of biotin moieties, phosphorothioate linkages and antigens. --

-- 147. (NEW) The modification of claim 117, further comprising a modification which allows capture of the displacer-recipient complex by affinity chromatography. --

-- 148. (NEW) An artificially constructed polynucleotide hybrid comprising a naturally occurring recipient polynucleotide duplex hybridized to the nucleic acid displacer composition of any one of claims 118-147. --

-- 149. (NEW) A process for modifying a recipient polynucleotide duplex comprising contacting under complex forming conditions such recipient polynucleotide duplex with the nucleic acid displacer composition of claim 118. --

-- 150. (NEW) The process of claim 149, wherein at least one of the nucleotides complementary to one strand of said recipient polynucleotide duplex is modified to increase the stability of the displacer-recipient complex. --

-- 151. (NEW) The process of claim 149, wherein at least one of the nucleotides complementary to one strand of a recipient polynucleotide duplex is modified to increase the melting temperature of the displacer-recipient complex. --

-- 152. (NEW) The process of claim 151, wherein said modified nucleotides comprise modified nucleotides which increase the association constant with the complementary nucleotides by at least about 20 percent. --

-- 153. (NEW) The process of claim 149, wherein said modification is in the second sequence of the displacer. --

-- 154. (NEW) The process of claim 153, wherein at least about 10% of the nucleotides in said second sequence is modified. --

-- 155. (NEW) The process of claim 153, wherein said modification comprises a modified base member selected from the group consisting of 5-halogenated pyrimidine nucleotides, 5-methyldeoxycytidine, diaminopurine deoxynucleotide, ribonucleotides, and 2'-alkylated ribonucleotides. --

-- 156. (NEW) The process of claim 153, wherein said modification is carried out on a modified nucleotide comprising 5-halogenated pyrimidine nucleotide. --

-- 157. (NEW) The process of claim 153, wherein said modification is carried out on a modified nucleotide comprising 5-bromodeoxyuridine. --

-- 158. (NEW) The process of claim 153, wherein said modification is carried out on a modified nucleotide comprising 5-methyldeoxycytidine. --

-- 159. (NEW) The process of claim 159, wherein said displacer contains at least one moiety attached to a terminus of the oligo or polynucleotide, said moiety conferring endonuclease resistance to the terminus to which it is attached. --

-- 160. (NEW) The process of claim 159, wherein said moiety is attached to a terminal nucleotide. --

-- 161. (NEW) The process of claim 159, wherein said moiety is indirectly attached to a terminal nucleotide. --

-- 162. (NEW) The process of claim 159, wherein said moiety is attached to the deoxyribose moiety at the hydroxyl group of a terminal nucleotide. --

-- 163. (NEW) The process of claim 159, wherein said moiety is attached to the phosphate moiety of a terminal nucleotide. --

-- 164. (NEW) The process of claim 159, wherein the moiety is selected from the group consisting of intercalating agents, isoureas, carbodiimides and N-hydroxybenzotriazoles. --

-- 165. (NEW) The process of claim 161, wherein said moiety is a methylthiophosphonate. --

-- 166. (NEW) The process of claim 161, wherein said moiety is selected from the group consisting of polypeptides and proteins. --

-- 167. (NEW) The process of claim 161, wherein said moiety comprises a 2',3'-dideoxyribose nucleotide attached to the 3'-terminal nucleotide through a phosphodiester linkage. --

-- 168. (NEW) The process of claim 167, wherein said 2',3'-dideoxyribose nucleotide comprises a modified 2',3'-dideoxyribose nucleotide. --

-- 169. (NEW) A process for labeling a displacer-recipient complex comprising contacting a recipient polynucleotide duplex with the displacer recited in claim 161 under complex forming conditions, wherein said displacer contains a modification which will permit detection of the displacer-recipient complex. --

-- 170. (NEW) The process of claim 169, wherein said modification comprises a member selected from the group consisting of radioactive labels, fluorescent and chemiluminescent labels, enzymes and targets for detection. --

-- 171. (NEW) The process of claim 169, wherein said modification comprises one or more targets for affinity chromatography. --

-- 172. (NEW) The process of claim 169, wherein said modification is selected from the group consisting of biotin moieties, antigens and phosphorothioate linkages. --

-- 173. (NEW) In a process for capturing an artificially constructed nucleic acid hybrid by affinity chromatography, the improvement comprising modifying the hybrid by the process of claim 149. --

-- 174. (NEW) In a process for enriching a recipient polynucleotide duplex in a population of polynucleotide duplexes, the improvement comprising labeling the recipient polynucleotide duplex by the process of claim 149. --

-- 175. (NEW) In a process for the site-specific addition, deletion or alteration of nucleotides in a recipient polynucleotide duplex, the improvement comprising modifying the duplex by the process of claim 149. --

-- 176. (NEW) In a process for repairing a mutational lesion comprising replacing a naturally occurring strand of nucleic acid with a modified strand of nucleic acid, the improvement comprising introducing said modified strand of nucleic acid to the naturally occurring duplex by the process of claim 149, and displacing said naturally occurring strand thereby. --

-- 177. (NEW) A process for site-specific addition, deletion or alteration of nucleotides in a recipient polynucleotide duplex in a cell, said process comprising the steps of:

i) providing said nucleic acid displacer composition of claim 117; and

ii) introducing said composition into said cell. --

-- 178. (NEW) A process for repairing a mutational lesion in a cell, said process comprising the steps of:

i) providing said nucleic acid displacer composition of claim 117; and

ii) introducing said composition into said cell. --

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REMARKS

In this new application which is a continuation of its allowed predecessor application (U.S. Serial No. 09/387,300, filed on August 31, 1999), Applicants are presenting new claims 117-178 for examination on the merits.

Information cross-referencing this continuation application with the previous parent application, Serial No. 09/387,300, filed on August 31, 1999, has been inserted on page 1 in the specification. As indicated above, the parent is allowed but has not yet been issued, although the issue fee is being concurrently authorized with the filing of this continuation application.

Applicants are also herewith submitting an Information Disclosure Statement (IDS) in order to present 37 documents for consideration by the Examiner.

If it would be helpful to expediting the processing of this continuation application, the undersigned attorney may be contacted during normal business hours at (212) 583-0100.

Entry of claims 117-178 is respectfully requested.

Favorable action on this application is further respectfully urged.

Respectfully submitted,

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